DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

95057d

Food and Drug Administration
Center for Devices and
Radiological Health
2098 Gaither Road
Rockville, MD 20850

OCT 8 2004

WARNING LETTER

VIA FEDERAL EXPRESS

Mr. Dennis J. Allingham
President and CEO
Lifecore Biomedical, Inc.
3515 Lyman Boulevard
Chaska, Minnesota 55318-3051

Dear Mr. Allingham:

During an inspection of your establishment located in Chaska, MN, on April 29 to May 17, 2004, our investigator determined that your firm manufactures hyaluronate-related products for ophthalmic and other uses, including post-operative adhesion reduction. Gynecare Intergel Adhesion Prevention Solution (Intergel) is a device within the meaning of section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act)(21 U.S.C.§ 321(h)).

The above-stated inspection revealed that your device, Intergel, is misbranded under section 502(t)(2) of the Act (21 U.S.C. 352(t)(2)), in that your firm failed to furnish material or information as required under section 519 of the Act and regulations implementing that section at Title 21 Code of Federal Regulations (21 CFR), Part 803 - Medical Device Reporting (MDR).

Specifically, for 11 separate events, Complaint #s H01-000063, H01-000064, H01-000065, H02-000001, H02-000080, H03-000011, H03-000029, H03-000042, H03-000054, H03-000089, and H03-000006, you failed to submit an MDR to the Food and Drug Administration (FDA) within 30 days of receiving information that reasonably suggested that one of your commercially distributed devices may have caused or contributed to a death or serious injury. [21 CFR 803.50(a)(1)]

For example, Complaint # H03-000054 documents an event involving a patient who underwent an operative laparoscopy and lysis of adhesions. 300 ml of Intergel was instilled at the end of the procedure. By post-op day three the

patient had developed severe abdominal pain with tachycardia, elevated temperature, and shortness of breath. The severe pain resolved in one week, but the patient's chronic pelvic pain persisted. A recent exam showed that the left side of the pelvis appeared frozen, reflecting serious adhesive disease. Your medical reviewer could not rule out the contribution of Intergel to this event. The information in the event record reasonably suggests that the use of this device may have caused or contributed to a reportable serious injury, as defined by 21 CFR 803.3(bb)(1)(ii). This event is reportable as a serious injury MDR.

Additionally, you failed to submit at least 2 MDRs for Complaints #H02-000095 and #H02-000074 to the FDA within 30 days of receiving or otherwise becoming aware of information that reasonably suggested that one of your commercially distributed devices has malfunctioned and would be likely to cause or contribute to a death or serious injury if the malfunction were to recur. [21 CFR 803.50(a)(2)].

Complaint # H02-000095 reports an event that occurred when a physician performed a laparoscopy and laparoscopic appendectomy on a patient and Intergel was instilled at the end of the procedure. One week post-op the patient was re-admitted with complications. A laparotomy was performed and a large abscess was removed. There was also an eschar covering over the intestine with inflammation of the intestinal serosa beneath. You became aware of the event on October 03, 2002. Your qualified medical professional determined that the infection and subsequent abscess could not have been caused by Intergel, but that Intergel was responsible for the eschar covering of the intestine. This event suggests that the device failed to perform as intended and should have been submitted to FDA as a malfunction MDR.

Based on our review of complaint #H02-000074, which the FDA investigator listed under observation #2 as requiring a serious injury MDR report, we concluded that an MDR malfunction report should have been submitted instead. Although the qualified medical professional's opinion was that the patient's pain may have been related to the hematoma and not the Intergel, he indicated that it is

possible that Intergel may not be as effective in the prevention of adhesions in the presence of blood. Due to the increase in the number of adhesions seen by the physician in the post op laparotomy, this event suggests that the device failed to perform as intended and should have been submitted to FDA as a malfunction MDR.

We acknowledge receipt of your written response to the FDA 483, dated May 28, 2004. Regarding the MDR issues, you state your firm continues to believe that the complaints listed on the FDA 483 under observations #2 and #3 are not required to be submitted as MDRs. With regard to the complaints listed under observation #2 (H02-000073, H02-000074, H03-000011, H03-000029, H03-000042, H03-000054, and H03-000089), you assert in your response that "[i]n each of the files identified by the FDA investigator (1) the event in question did not involve a serious injury as defined in 21 CFR §803.3(bb), or (2) a qualified medical professional reached a reasonable conclusion that INTERGEL did not cause or contribute to serious injury and thus the event was not reportable pursuant to 21 CFR § 803.20(c)(2)."

Your response to this inspectional observation is not adequate. After carefully reviewing the complaints and other documentation pertaining to the events listed in observation #2, we determined that five of the seven complaints, (#H03-000011, #H03-000029, #H03-000042, #H03-000054 and #H03-000089), should have been reported to FDA as serious injury MDR reports in accordance with 21 CFR 803.50(a)(1). Each of these complaints involved serious injuries within the meaning of 21 CFR 803.3(bb)(1) in that they either resulted in permanent impairment of a body function or permanent damage to a body structure, or they necessitated medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure. We agree with your conclusion that Complaint #H02-000073 is not an MDR reportable event.

With regard to the complaints listed under observation #3 (H02-000095 and H03-000023), you state in your response that no MDR reports were required for these events because your product performed as intended and therefore did not malfunction.

After reviewing the complaints listed in FDA 483 observation #3, we agree that one of the two complaints listed is not a reportable MDR Malfunction (H03-000023). However, our review revealed that the other complaint, H03-000095, dated October 03, 2002, is a reportable MDR malfunction under 21 CFR 803.50(a)(2). Your response regarding complaint #H02-000095 states that the qualified medical professionals' finding that Intergel was likely responsible for the coating of the intestine was consistent with Intergel's labeling and therefore did not represent a malfunction. The device description section of Intergel's approved labeling describes the device as a solution that "provides a transient viscous, lubricious coating on the peritoneal surfaces following surgical procedures". However, an eschar covering over the intestine that, as described in the complaint, "peeled away easily and revealed inflammation of the intestinal serosa," does not meet the device description as stated in the labeling and, therefore, reasonably suggests that your device has malfunctioned.

In your May 28, 2004 response letter, you requested a meeting with FDA representatives to discuss the MDR-related 483 observations with regard to the application of 21 CFR 803.20 (c)(2) which provides that MDR reports do not need to be submitted for events for which there is information that would cause a qualified medical professional to reach a reasonable conclusion that a device did not cause or contribute to a death or serious injury, or that a malfunction would not be likely to cause or contribute to a death or serious injury if it were to recur. On September 02, 2004, we held a teleconference with you. During that teleconference, we discussed our interpretation of 21 CFR 803.20(c)(2). As we stated during the teleconference, the medical professional reviewing complaints for MDR reportability must stay within the confines of 21 CFR Part 803 and use the regulation to make a decision based on the definitions in the regulation. We also emphasized that, when making determinations concerning MDR reportability, FDA considers the entire complaint event record along with any related information that is available.

This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence to each applicable requirement of the

Act and regulations. Federal agencies are advised of the issuance of all Warning Letters about devices so that they may take this information into account when considering the award of contracts.

You should take prompt action to correct the deviations described above. Failure to promptly correct these deviations may result in regulatory action being initiated without further notice. These actions include, but are not limited to, seizure, injunction, and/or civil money penalties.

Please notify this office in writing within fifteen (15) working days of your receipt of this letter, of the specific steps you have taken or will take to correct the noted violations. Be sure to include an explanation of the steps you are taking to prevent the recurrence of similar violations in the future. If corrective action cannot be completed within 15 working days, state the reason for the delay and the time frame within which the corrections will be completed.

Your response should be sent to Paul Tilton, Chief, OB/GYN, Gastroenterology and Urology Devices Branch, HFZ-332, Division of Enforcement A, Center for Devices and Radiological Health, Food and Drug Administration, 2098 Gaither Road, Rockville, Maryland 20850. If you have any questions about the contents of this letter please contact Mr. Tilton at (240) 276-0115.

Sincerely yours,

Timothy A. Ulatowski
Director
Office of Compliance
Center for Devices and
Radiological Health